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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/865,950	05/25/2001	Manoussos Perros	PC10925A	6657

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EXAMINER	
HUANG, EVELYN MEI	
ART UNIT	PAPER NUMBER
1625	3

DATE MAILED: 01/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/865,950	Applicant(s) PERROS ET AL.	
	Examiner Evelyn Huang	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,19-22 and 38-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,19-22 and 38-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. Claims 1-9, 19-22, 38-56 are pending. Claims 10-18, 23-37 have been canceled according to the preliminary amendment filed on 5-25-2001.

Claim Rejections - 35 USC § 112(2)

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19, 20, 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 19, it is unclear whether the instant compound 'modulates' the CCR5 receptor. The term 'modulation' includes agonism and antagonism of the receptors, thereby leading to different sets of physiological responses, which are not described in the specification.

b. The term "genetically related" in claim 20 is a relative term which renders the claim indefinite. The degree of homology required to be considered "genetically related" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

c. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83

USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 22 recites the broad recitation 'graft rejection', and the claim also recites 'kidney or a lung allograft', which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following evaluation factors have been considered

a. *Nature of the invention.*

The instant invention is drawn to a triazolyl-tropane compound for use in the treatment of a disorder in which modulation of a CCR5 receptor is implicated; the disorders are recited on pages 29-31 of the specification.

b. *State of the prior art and the level of the skill in the art.*

Chemokine receptors exist in several subtypes. While many diseases are implicated to be mediated by the chemokine receptors, the particular responses elicited by each subtype have not been delineated. A substituted aryl-piperazine compound has been described to have binding affinity to the chemokine receptor (Mills, WO 98/25627, cited by the applicant). Several small molecule antagonists of chemokine receptor have also been described (Hesselgesser, page 15689), however, the instant compound does not resemble any of these prior art compounds.

It is well recognized in the art that the binding data do not distinguish the agonists from the antagonists of the chemokine receptor, nor the physiological conditions requiring the activation of an agonist and those requiring the action of an antagonists.

The level of the skilled in the chemokine receptor art is high.

c. *Predictability/unpredictability of the art.*

The high degree of unpredictability is well recognized in the chemokine receptor ligand art. A small change in the structure would drastically affect its biological activity as evidenced in the different K_i values for the structurally similar compounds (Hesselgesser, page 15689). Since the in vitro result is highly unpredictable, the degree of unpredictability in the much more complex *in vivo* situation would be expected to be even greater.

d. *Amount of guidance/working examples.*

The preparation of example compounds has been described.

The reference for the procedure for assessing the inhibition of CCR5 binding is found on page 62. The result is described as 'all the tested compounds were found to have an IC_{50} values of less than 10 nM'. No *in vivo* procedures are described.

e. *The breadth of the claims.*

Applicant's assertion that all the inventive compounds would be effective in treating a disorder in which modulation (including agonism and antagonism) of a CCR5 receptor is implicated, and useful in treating diseases of various origins and etiology, including any types of renal diseases, AIDS etc., does not commensurate with the scope of the objective enablement, especially in view of the fact that the binding data does not distinguish an agonist from the antagonist, the high degree of unpredictability and the absence of working examples directed to specific compounds (paragraphs c, d above).

f. *Quantitation of undue experimentation.*

Since sufficient teaching and guidance have been provided in the disclosure, one of ordinary skill in the art, even with high degree of skill, would not be able to use the all the compound as claimed without undue experimentation, especially when at present, there is no umbrella drug compound that would treat all the diseases as recited in the instant claims.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible

harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-9, 19-22, 38-56 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the corresponding claims of U.S. Application No. 09/454578. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant compound, its composition and method of use are encompassed by the copending claims. To one of ordinary skill in the art, choosing one among many is prima facie obvious in the absence of unexpected results.

Allowable Subject Matter

5. The subject matter of claims 1-9, 38-56 are allowable.

The closest prior art is Urch (5968947) wherein the instant is generically disclosed. The triazolyl of the instant, however, is not described by Urch. Motivation to modify Urch's compound to arrive at the instant is lacking.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 703-305-7247. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat can be reached on 703-308-2439. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Evelyn Huang
Primary Examiner
Art Unit 1625

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January 3, 2002